REMARKS

Claims 1-3, 21, and 22 are pending. No claims have been allowed.

Claim 1 has been amended to recite a composition for treating horses infected with *Sarcocystis neurona* comprising a mixture of isolated antibodies against a 16 ±4 kDa antigen of *Sarcocystis neurona* and isolated antibodies against a 30 ±4 kDa antigen of *Sarcocystis neurona*. Support for the amendment can be found in the paragraph bridging pages 26-27. The term "vaccine" was replaced with the term "composition." A vaccine comprising antibodies against the 16 and 30 kDa antigens is a composition comprising antibodies against the 16 and 30 kDa antigens. This view is also supported by the Examiner in Paper No. 6, page 4.

Claims 1 and 21 have also been amended to recite that the composition and method for using are for treating an equid infected with *Sarcocystis neurona*. This therapeutic use for the vaccine is supported by the specification on page 15, lines 11-15. Claims 2 and 3 were amended to be consistent with Claim 1.

1. Claims 1-3, 21, and 22 remain rejected under 35 U.S.C. § 112, first paragraph.

The applicants believe that the specification

provides enablement which is reasonably commensurate with the scope of presently amended Claims 1-3, 21, and 22.

The presently amended claims provide a composition comprising a mixture of isolated antibodies against the 16 ±4 and 30 ±4 kDa antigens for treating horses infected with *Sarcocystis neurona* (Claims 1-3) and method for treating (Claims 21-22). When all of the evidence relating to the factors set forth in M.P.E.P. § 2164.01(a) for determining whether a disclosure satisfies the enablement requirement is considered, the evidence as a whole shows that the scope of the applicants' presently amended claims is enabled by the applicants' disclosure.

The applicants' specification teaches that *Sarcocystis neurona* possesses a 16 ±4 and a 30 ±4 kDa antigen, both which are specific to *Sarcocystis neurona*, and which are useful for producing vaccines (specification: page 13, lines 16-23). The applicants teach a variety of ways for vaccinating horses (specification: page 13, lines 24-35), teaches that the vaccines can comprise antibodies (specification: page 15, lines 13-15), and teaches how to make polyclonal antibodies (specification: para. bridging pages 26-27) and monoclonal antibodies (specification: page 27, lines 4-22; Example 1) for the vaccines. The applicants teach

that antibody vaccines can be used for therapeutic treatment of horses infected with *Sarcocystis neurona* (specification: page 15, lines 11-15) and to provide passive immunity (specification: page 26, lines 20-26).

Liang (1998) provides an idea of what the state of the art was at about the time of the applicants' invention. Liang (1998) teaches that antisera from horses with EPM contain antibodies against 11, 14, 16, and 30 kDa antigens. Liang (1998) also teaches that *Sarcocystis neurona* "was sensitive to specific antibodies but that "a 10-min exposure to antiserum was required to yield significant reduction in parasite production" (Liang (1998): page 1837, right col.). Liang (1998) further teaches that protective antibodies against some apicomplexan parasites may be effective *in vitro* but ineffective *in vivo* which Liang (1998) cites Hines *et al.* (Inf. Immun. 63 349-352 (1995); copy enclosed) for support.

Hines showed that immunizing cattle with a vaccine containing the MSA-1 antigen of *Babesia bovis* failed to protect the immunized cattle against challenge with *Babesia bovis*. However, Hines suggested that an efficacious vaccine would include at least a second antigen of *Babesia bovis* as was shown in the case of a malaria vaccine which contained two antigens and which was shown to be effective *in vivo* against the malaria

parasite whereas a vaccine containing only one of the antigens was partially effective (Hines: page 351, second para.). The applicants' claimed composition contains antibodies against a second antigen.

Liang (1998) also teaches that "[t]he high rate of exposure [of horses] to *Sarcocystis neurona* and the relatively low incidence of clinical EPM indicate that most horses develop effective immunity that may prevent entry into the central nervous system [citing various sources]" (Liang (1998): page 1834, right col.). Liang (1998) also teaches that antisera from horses with EPM have antibodies against several *Sarcocystis neurona* antigens, in particular the 16 and 30 kDa antigens. Liang (1998) identifies the 11, 14, 16, and 30 as major immunogens (Liang (1998): Figure 1). Liang (1998) further teaches that antibodies against the 30 kDa antigen are not recognized as specific (Liang (1998): page 1837, left col., first para.), which suggests that the 30 kDa antigen is common to all *Sarcocystis* spp. and not unique to *Sarcocystis neurona*. However, the applicants teach that antisera from horses infected with *Sarcocystis neurona* contain antibodies specific for the 30 kDa antigen of *Sarcocystis neurona*. Therefore, since many horses exposed to *Sarcocystis neurona* do not have clinical signs of EPM but have immunity to *Sarcocystis neurona*, Liang (1998) teaches that the major immunogens

of *Sarcocystis neurona* infected horses comprise the 16 and 30 kDa antigens, and the applicants teach that horses make antibodies specific to the 30 ±4 kDa antigen, there is a nexus between the 16 and 30 kDa-specific antibodies identified in Liang and by the applicants and a composition comprising the 16 ±4 and 30 ±4 kDa antigens for treating horses infected with *Sarcocystis neurona*.

Liang (1998) provides further support for a nexus between the 16 ±4 and 30 ±4 kDa-specific antibodies and their use in a composition for treating horses infected with *Sarcocystis neurona*. Liang (1998) teaches that the 14, 16, and 30 kDa antigens are surface antigens (Liang (1998): page 1836, left col., and Figure 3). Because surface antigens are generally important in the function or life-cycle of the organism, it is reasonable to expect that blocking the activity of one or more surface antigens by binding the antigens with antibodies would interrupt the function or life-cycle of the *Sarcocystis neurona*. Therefore, the applicants' presently claimed composition, which would bind to the 16 ±4 and 30 ±4 kDa antigens, would be expected to have at least some efficacy in treating horses infected with *Sarcocystis neurona*.

While Liang (1998) teaches that a "10-minute exposure to antiserum was required to yield a

significant reduction in parasite production" and that "may partially explain why protective antibodies to some apicomplexan parasites are effective in vitro but not in vivo" (Liang (1998): page 1837, left col., third para.), Liang (1998) suggests that the reason is that "newly released parasites are exposed to serum for a shorter time in vivo, and the access of neutralization-sensitive epitopes to antibody may be limited" and that "[m]erozoites in vivo may move more directly from cell to cell" (Liang (1998): page 1837, left col., third para.). While the statements suggest that humoral responses to *Sarcocystis neurona* may be of limited efficacy in inhibiting parasite production, the statements do not suggest that humoral responses would have no efficacy against disease caused by *Sarcocystis neurona*. In fact, Liang (1998) suggests that antibodies against the 14 and 16 kDa antigens may be efficacious against the EPM disease caused by *Sarcocystis neurona* because Liang (1998) also teaches that "in the case of EPM, disease occurs only after the merozoite passes through the vascular endothelium of the blood-brain barrier into the central nervous system, and so humoral responses may play an essential role in blocking this migration" (Liang (1998): page 1837, left col., third para.) particularly since "specific cytotoxic T-cells are ineffective in attacking merozoites migrating to the

central nervous system in the bloodstream" (Liang (1998): page 1837, left col., third para.). Liang (1998) further suggests that the 14 and 16 kDa antigens may be useful components of a subunit vaccine. Thus, the above suggests that the applicants' claimed composition comprising antibodies against the 16 ±4 and 30 ±4 kDa antigens might provide an efficacious means for treating horses infected with *Sarcocystis neurona*.

Therefore, in light of the above, the state of the art reasonably suggests that the applicants' claimed composition comprising a mixture of antibodies against several *Sarcocystis neurona* antigens would likely be efficacious for treating horses infected with *Sarcocystis neurona*. While the efficacy of a composition comprising a single antibody against a single antigen might be unpredictable, in light of the state of the art, one skilled in the art would likely predict that a composition comprising a mixture of antibodies against several antigens (16 ±4 and 30 ±4 kDa antigens) would provide an efficacious treatment for horses infected with *Sarcocystis neurona*.

Further, while the applicants do not provide working examples showing that their claimed composition provides an efficacious treatment for horses infected with *Sarcocystis neurona*, the applicants' disclosure in light of the state of the art suggests that the

applicants' claimed composition would be useful for treating horses infected with *Sarcocystis neurona*. The only experimentation expected would be adjusting the amounts of each antibody in the composition. Such experimentation is routine and would be performed by one skilled in the art even if the applicants had provided working examples.

Therefore, in light of the above, the scope of presently amended Claims 1-3, 21, and 22 are believed to be reasonably enabled by the applicants' disclosure. Reconsideration of the rejection is requested.

2. Claims 1-3 were rejected under 35 U.S.C. § 102(b) as being anticipated by Liang (1998).

Claim 1 has been amended to recite a composition comprising a mixture of isolated antibodies against the 16 ±4 and 30 ±4 kDa antigens. The amendment distinguishes the applicants' claimed composition from the composition disclosed in Liang (1998).

The Liang (1998) composition does not contain isolated antibodies against the 16 ±4 and 30 ±4 kDa antigens. The Liang (1998) composition is serum or CFS collected from a horse with EPM. Because horses with EPM are infected with the whole, living parasite, the serum or CFS would be expected to contain antibodies against other *Sarcocystis neurona* antigens in addition

to antibodies against the 16 ±4 and 30 ±4 kDa antigens. This can be seen in Figure 1 of Liang (1998) which shows that most sera or CFS from horses with EPM contain antibodies against other *Sarcocystis neurona* antigens in addition to the 16 and 30 kDa antigens. The serum or CFS would also likely contain antibodies against related *Sarcocystis* spp. (*See* U.S. Patent 6,153,394 to Mansfield *et al.* which says that serum or CFS from horses with EPM contains cross-reacting antibodies against other *Sarcocystis* spp.). The serum or CFS might also contain infectious *Sarcocystis neurona* or other *Sarcocystis* spp. which would render the composition useless as a vaccine. Because of the risk that serum or CFS from horses might contain infectious parasite, the serum or CFS would not be used to treat horses. Furthermore, because the serum or CFS from horses does not always contain antibodies against both the 16 and 30 kDa antigens (Liang (1998): Figures 1 and 2), there is no way to predict whether serum or CFS from a particular horse contains antibodies against both antigens.

In contrast to the serum or CFS from a horse with EPM, the applicants' presently claimed composition comprises a mixture of isolated anti-*Sarcocystis neurona* antibodies against the 16 ±4 and 30 ±4 kDa antigens. The presently claimed composition always contains antibodies against both the 16 ±4 and 30 ±4 kDa

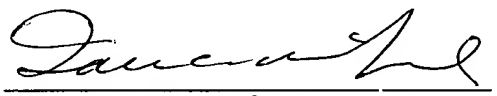
antigens. The presently claimed composition does not contain antibodies against other *Sarcocystis neurona* antigens except those which may be mixed with the antibodies against the 16 ±4 and 30 ±4 kDa antigens. The presently claimed composition does not contain antibodies against other *Sarcocystis* spp. Most importantly, the presently claimed composition does not contain infectious *Sarcocystis neurona* or other *Sarcocystis* spp.

In light of the above, presently amended Claims 1-3 are not believed to be anticipated by Liang (1998). Reconsideration of the rejection is requested.

Attached hereto is a marked-up version of the changes made to the claims by the current amendment. The attachment is captioned "**VERSION WITH MARKINGS TO SHOW CHANGES MADE**."

In view of the above, it is believed that Claims 1-3, 21, and 22 are in form for allowance. Notice of allowance is requested.

Respectfully,



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Encl. Hines *et al.*, Inf. Immun. 63: 349-352 (1995)

VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Claims:

Claims 1, 2, 3, and 21 were amended as follows.

-1- (Twice amended)

A [vaccine] composition for [providing passive protection to an individual] treating an equid infected with *Sarcocystis neurona* comprising a mixture of isolated antibodies [which are] against a 16 [±4] ±4 kDa antigen of *Sarcocystis neurona* and isolated antibodies against a 30 [±4] ±4 kDa antigen of *Sarcocystis neurona* [both of which are specific to *Sarcocystis neurona*].

-2- (Amended)

The [vaccine] composition of Claim 1 wherein the antibodies are selected from the group consisting of polyclonal antibodies and monoclonal antibodies.

-3- (Amended)

The [vaccine] composition of claim 1 wherein the [vaccine] composition is provided in a pharmaceutically accepted carrier.

A method for [providing passive protection to] <u>treating</u> an equid infected with *Sarcocystis neurona* comprising:

(a) providing antibodies against a 16 [±4] <u>±4</u> kDa antigen and a 30 [±4] <u>±4</u> kDa antigen both of which are specific to *Sarcocystis neurona* wherein the antibodies are selected from the group consisting of polyclonal antibodies and monoclonal antibodies; and

(b) inoculating the equid with the antibodies to [provide the passive protection to] <u>treat</u> the equid.